Remarks

Claim Rejections Under 35 U.S.C. §112, First Paragraph-Written Description

The Examiner has rejected claims 1-7 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner is concerned that the specification does not sufficiently show that applicant was in possession of the claimed genus of molecules. It appears to be the opinion of the Examiner that the written description only reasonably conveys a drug delivery composition comprising one species of the anticancer agent (CPT), one species of a suppressor of antiapoptotic cellular defense (BH3), one species of a cell-surface targeting moiety (LHRH), and one species of a multifunctional carrier (PEG).

The present invention is directed to a complex drug delivery composition, a method of using the composition for treating cancer and a method of preparing the composition. As recited in new independent claim 8, the composition includes a complex conjugate of the following components: an anticancer agent; a poly(ethylene glycol) polymer; and at least one of a BH3 peptide and luteinizing hormone-releasing hormone (LHRH). Applicants submit that the skilled artisan would clearly envision the chemical structure of this drug delivery composition.

The purpose of the present invention is to provide an improved means of treating cancer with traditional anticancer agents. In particular, the purpose is to enhance the delivery of the anticancer agent to cancer *via* a targeted delivery approach where anticancer agent-PEG conjugates are specifically targeted to the cancer cell surface and/or intracellular antiapoptic cellular defense pathways using LHRH and/or BH3 peptide, respectively, as components of the conjugates. This is described, for example, on page 9, lines 17-26, and page 12, lines 19-26 to page 13, line 1 of the application.

With respect to the anticancer agent component, it is submitted that Applicants, along with other experts in the drug delivery field, are concerned with improved delivery of traditional

pharmaceuticals. The important features of the invention lie in how to achieve targeted delivery of traditional anticancer agents, and not in the identity of the anticancer agent component itself. As set forth in the present specification, any number of pharmaceuticals are useful for treating cancer, and the pharmaceutical to be delivered would depend upon the cancer being treating. See, for example, page 19, lines 7-32, page 20, lines 1-32 and page 21, lines 1 and 2 of the application. Moreover, this information would be well known to the skilled clinician. Applicants' working examples include CPT as an exemplary anticancer agent for incorporation into a targeted drug delivery system of the present invention. However, a skilled artisan would clearly recognize that the invention is not limited to this drug. Moreover, the level of skill and knowledge in the art is high, and the specification provides sufficient disclosure for the skilled artisan to incorporate traditional anticancer agents other than CPT into a system of the present invention.

In view of the amendments and remarks presented herewith, Applicants submit that the written description requirement has been met with respect to new independent claim 8, as well as the remaining claims, which depend either directly or indirectly therefrom. Therefore, withdrawal of these rejections is respectfully requested.

Claim Rejections Under 35 U.S.C. §112, First Paragraph-Enablement

The Examiner has also rejected claims 1-7 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner states that the claims may read on a drug delivery composition for treating cancer, wherein the composition includes a cell-surface targeting moiety and a multifunctional carrier that may or may not be the same. The Examiner appears to be concerned about the anticancer effectiveness of a drug delivery composition where the cell-surface targeting moiety and the multifunctional carrier are the same.

As set forth in new independent claim 8, the present invention is directed in part to a drug delivery composition for treating cancer that includes an anticancer agent; a poly(ethylene

glycol) polymer; and at least one of a BH3 peptide and luteinizing hormone-releasing hormone (LHRH). Therefore, the cell-surface targeting moiety and multifunctional carrier are different components. The remaining claims depend either directly or indirectly from claim 8.

In view of the amendments and remarks presented herewith, Applicants submit that the enablement requirement has been met with respect to new independent claim 8 and the remaining claims depending therefrom. Therefore, withdrawal of these rejections is respectfully requested.

Claim Rejections Under 35 U.S.C. §102

Minko, et al.

The Examiner has rejected claims 1-7 under 35 U.S.C. §102(b) as being allegedly anticipated by Minko, et al. (Int. J. Cancer 2000; 86:108-117). In particular, the Examiner alleges that Minko, et al. teach a drug delivery composition for treating cancer comprising the anticancer agent doxorubicin (DOX) linked through an oligopeptide spacer to a HPMA copolymer carrier.

As set forth in the amended claims, the drug delivery composition of the present invention includes an anticancer agent; a poly(ethylene glycol) polymer; and at least one of a BH3 peptide and luteinizing hormone-releasing hormone (LHRH). The cited Minko reference does not disclose or suggest such a composition. For example, there is no disclosure or suggestion in the Minko reference to provide a conjugate including an anticancer agent in combination with either BH3 peptide and/or LHRH as a means of achieving targeted delivery of the anticancer agent to cancer, nor to use a PEG polymer as a carrier.

Since the Minko reference fails to teach each and every element of the claimed invention as set forth in independent claim 8, Applicants submit that claim 8 and the claims depending therefrom are patentable thereover. Therefore, withdrawal of these rejections is respectfully requested.

Lu, et al.

The examiner has also rejected claims 1-7 under 35 U.S.C. §102(b) as being allegedly anticipated by Lu, et al. (J. Controlled Rel. 1/17/2002;78: 165-173). In particular, the Examiner states that the abstract of the Lu, et al. reference discloses a drug delivery composition for treating cancer that includes a polymerizable carrier antibody Fab' fragment as the targeting agent linked to an anticancer agent, such as mesochlorin e_6. The Examiner further states that the polymerizable antibody fragments were prepared by polymerizing an antibody fragment including a spacer, such as PEG, with HPMA.

As presently recited in independent claim 8, the instant drug delivery composition includes LHRH and/or BH3 peptide. These components specifically target the drug to the cancer cell surface and/or intracellular antiapoptic cellular defense pathways, respectively. Lu, et al. fail to disclose or suggest such a composition. Since Lu, et al. fail to teach each and every element of the invention as recited in independent claim 8, Applicants submit that claim 8 and its dependent claims are patentable over this reference. Withdrawal of these rejections is respectfully requested.

Trouet, et al.

The Examiner has further rejected claims 1-7 under 35 U.S.C. §102(b) as being allegedly anticipated by Trouet, et al. (WO 01/91798, 2001). In particular, the Examiner states that Trouet, et al. teach a prodrug for treating cancer that includes a biologically active entity linked to a masking moiety *via* a linking moiety. The Examiner further states that the biologically active entity includes, but is not limited to, BH3 peptides and anticancer agents, that the linking moiety is preferably a peptide, and that the masking moiety may include large molecular weight biologically inert molecules, such as PEG or HPMA.

As set forth in the amended claims, the drug delivery composition of the present invention includes an anticancer agent; a poly(ethylene glycol) polymer; and at least one of a

BH3 peptide and luteinizing hormone-releasing hormone (LHRH). The Trouet reference does not disclose or suggest such a composition. For example, in contrast to the present invention, there is no disclosure or suggestion in the Trouet reference to provide a conjugate including an anticancer agent and either BH3 peptide and/or LHRH as a means of achieving targeted delivery of the anticancer agent to cancer. At best, Trouet, et al. suggest using either an anticancer agent or a BH3 peptide as the biologically active entity in claim 51. As described above, in the present invention, the BH3 peptide and LHRH are used to specifically target the PEG-carried anticancer agent to the cancer cell surface and/or intracellular antiapoptic cellular defense pathways, respectively. This is neither taught nor suggested by Trouet, et al.

Since the Trouet reference fails to teach each and every element of the invention set forth in independent claim 8, Applicants submit that claim 8 and its dependent claims are patentable over this reference. Withdrawal of these rejections is therefore respectfully requested.

Summary

Applicants submit that the claims as submitted are patentably distinct over the art and allowable in form, and an allowance of the claims is respectfully solicited. Should the Examiner have any questions regarding this response, the Examiner is encouraged to contact the undersigned at the telephone number set forth below.

Respectfully submitted,

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